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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/808,407	03/14/2001	Takuro Tamura	033808/027 8720	3695

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EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 08/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/808,407	TAMURA ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/2/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

1. This application has been transferred from Examiner Jeffrey Siew to Examiner Cynthia Wilder of Art Unit 1637. All future correspondence should be directed to Examiner Cynthia Wilder whose contact information appears at the end of this Office Action.

2. Applicant's amendment filed on June 2, 2004 is acknowledged and has been entered. Claims 1-5 have been amended. Claim 8 has been added. Claims 1-8 are pending. All of the amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on June 2, 2004 after the first Office action is acknowledged and entered. The Examiner has considered the IDS and a signed copy of the form-1449 is submitted with this Office action.

Sequence Compliance

5. Applicants' submission on June 2, 2004 of a raw sequence listing and computer readable format (CRF) is acknowledged and has been entered. However, it is noted that the each sequence recited in the specification and drawing as indicated by the raw sequence listing and

CFR is required to be identified by a proper sequence identifier (**SEQ ID NO:**) (see MPEP§ 2422.03). Appropriate correction is required.

Previous Rejections

6. The prior art rejection under 35 USC 102(b) directed to claim 1 as being anticipated by Lockhart et al is maintained and discussed below. The prior art rejection under 35 USC 103(a) directed to claims 2-7 as being unpatentable over Lockhart et al in view of Pal[1] is maintained and discussed below.

Claim Rejections - 35 USC § 102(b)

7. Once again, claim 1 is rejected under 35 USC 102(b) as being anticipated by Lockhart et al (Nature Biotechnology, vol. 14, pages 1675-1680, December 1996). Regarding claim 1, Lockhart et al teach a method of displaying results in which a plurality of probe biopolymers immobilized on a chip are hybridized to a sample biopolymers comprising step of displaying information obtained in hybridization experiments about a hybridization level for each probe (see whole document teaching arrays with measuring level of hybridization signal (see figure 3 and 5 and their teaching of phycoerythrin and fluorescein emission in experimental protocol). Lockhart et al teach that the array contains over 65,000 different oligonucleotide probes (see page 1678). Lockhart et al teach that in quantitative scan of the array the, the image is reduced to text file with position and intensity information which is merged with information relating to physical position on array of probe sequence and identity of sequences (see page 1679). The

[1] It is noted that Applicant was notified in a telephone interview on March 1, 2004, that the 103 rejection title sentence incorrectly states the secondary reference as Zho et al, where in fact the secondary reference is Pal et al (US 6,528,264) as recited in the body of the rejection and in the PTO-892. Accordingly, Lockhart in view of Pal et al is addressed in this Final Action.

term similarity score reads broadly and does not necessarily include a limitation of any type of algorithmic scoring program. In an array with unique probes wherein each probe is unique, each different probe may be interpreted to have no similarity. Therefore, Lockhart et al meets the limitation of claim 1 of the instant invention.

Claim Rejections - 35 USC § 103

8. Once again, Claims 2-7 are rejected under 35 USC 103(a) as being unpatentable over Lockhart et al (Nature Biotechnology, vol. 14, pages 1675-1680, December 1996) in view of Pal et al (6,528,264). The teachings of Lockhart et al are described previously. Regarding claims 2-7, Lockhart et al do not teach color assignment in display or multiple chips.

Pal et al teach displaying intensity of signals with color differentiation and comparing different biochips (see Figures 3A-D & col. 6, lines 24-36 and Figures 6A-6D). One of ordinary skill in the art would have been motivated to apply Pal et al's multiple chips and color display to Lockhart et al's microarray in order to visualize differences of hybridization against a plurality of different samples. It would have been *prima facie* obvious to apply Pal's et al multiple chips and color display to Lockhart et al's method of expression order to analyze many different samples with facility of visually distinguishing the sequence similarity.

Applicants' Traversal

9. Applicants' traverse the rejections on the following grounds: Applicants summarize the Examiner's rejection and asserts that the present invention as now claimed is directed to a method for displaying results of a hybridization experiment in which a plurality of probe

biopolymers immobilized on a biochip are hybridized to a sample biopolymers. Applicants state that the method incorporates the steps of determining information obtained in the hybridization experiment about a hybridization level for each of the probe biopolymers; determining a probe similarity score representing a similarity between first probe data on a base sequence of at least one of the probe biopolymers and second probe data on a base sequence of at least one other of the probe biopolymers ("a similarity score representing the similarity of base sequences between each of the probe biopolymers) and displaying the information about the level of hybridization for each of the probe biopolymers together with the probe similarity score, including generating a visually intuitive graphical representation of the determined hybridization level and correspondingly determined probe similarity score so as to provide at least one of a visual confirmation of similarities between the base sequences of corresponding biopolymers used in the hybridization experiments and a visual indication of unexpected or improper hybridization. Applicants state that the specification teaches that "In biochips that use longer DNA molecule, such as cDNA, as a probe biopolymer, no effective technique is know that can evaluate the results of hybridization using DNA sequence data" (page 3, lines 3-6). Applicants assert that the yeast expression analysis conducted by P. Brown's group if the Stanford University merely cluster probes so as to display a cluster tree diagram and indicates a hybridization level between Probe A and a sample B (probe vs. sample), but not similarity level between any two probes (probe vs. probe). Applicants state that the specification teaches that "No practical approach is known for determining if a probe biopolymer has been accurately hybridized to a sample biopolymer of interest and accordingly there is a need for such a method "(page 4, lines 19-22). Applicant contends that as such, the inventions is specifically directed to displaying the probe

similarity score, probe biopolymer data and hybridization level data are displayed side by side so as to compare with each other in a manner that is visually easy to understand. Applicants state that the probe similarity score is represented by square patterns having varying color depths, so as to make the displayed image, and consequently the information being represented, more visually intuitive. Applicants state that as shown in the attached explanatory drawing, the invention measures displays similarity levels between probes A immobilized on a biochip, rather than between a probe A and a sample B (not directly immobilized on the biochip, but hybridized with the probe A). Applicants state that taking figure 18 as an example (claim 7), the similarity pattern matrix 901 shows that probe 1 and Probe 2 have very similar physical DNA sequences but the tree diagram 1001 indicates that the probes have rather different homology properties from one another (Probe 1 is more closely related to probe 4). Applicant states that this suggests that the hybridization level data reflect the physical similarity of the DNA probe 1 and 2, rather than reflect their homologous similarity present in the sample DNA). Applicant states that in other words, the sample DNA molecules of the same type bind to two different types of DNA probes 1 and 2 that are very similar to one another, i.e., unintended hybridization of miss-hybridization. Accordingly, the invention "determines if unintended hybridization has occurred by observing the hybridization level information in the proximity of the object probe. Applicants state, "Also by selecting the information to be displayed with the similarity score matrix, the verification of the accuracy of the hybridization is possible in wider ranges". Applicants contend that Lockhart fails to teach or suggest at least "determining a probe similarity score representing a similarity between first probe data on a base sequence of at least one probe biopolymer and second probe data on a base sequence of at least one other of the probe

biopolymers so as to provide a visual indication of unexpected or improper hybridization according to the invention. Applicant asserts that in contrast, Lockhart merely quantitatively relates hybridization intensities of mRNAs, i.e., samples, to arrays of synthetic oligonucleotides, i.e., probes (**sample vs. probe**) rather any similarity levels between probes immobilized on a biochip (**probe vs. probe**). Applicant states that Lockhart does not disclose, teach or suggest at least displaying the "probe similarity score", along with the hybridization levels or intensities as disclosed or claimed for the present invention. Applicants state that Pal was relied upon by the Examiner to teach displaying intensity of signals with color differentiation and comparing different biochips. Applicants assert that Pal fails to compensate for Lockhart's deficiencies since Pal does not disclose, teach or suggest at least displaying the "probe similarity score" along with the hybridization levels or intensities as disclosed or claimed for the present invention. Applicant states that Pal merely uses false color fluorescence imaging to demonstrate the effectiveness of a substrate to retain DNA, hybridize DNA and provide acceptable signal to noise ratio. Applicant states that the different colors are selected in a convention to indicate relative levels of probe retention and hybridization. Pal does not display the "probe similarity score along with hybridization intensity of probes with color differentiation". Applicant state neither Lockhart nor Pal discloses, teaches or suggests the generating of a visually-intuitive graphical representation of the determined hybridization level and correspondingly determined probe similarity score nor the providing of a visual confirmation of similarities between the base sequences of corresponding biopolymers used in the hybridization experiment or a visual indication of unexpected or improper hybridization. Applicants assert that Lockhart by itself does not show or suggest such features, while Pal merely shows a crude mechanism based on

false color fluorescence to visually differentiate its results. The combination of these references would fall short of embodying a method having every feature of the present invention as claimed, most especially the features noted above. Applicant states that further, since claims 2-7 recite features in addition to those in independent claim 1 that are already not shown by the cited prior art, these same references cannot be used to render obvious the more specific features of dependent claims 2-7. Applicants state that rather the present invention as a whole is distinguished and thereby allowable over the prior art.

Applicant states that although the invention applies general homology analysis, such as Smith-Waterman method or BLAST, the invention applies the homology analysis between probes rather than between a probe and a sample to achieve unexpected results or properties. Applicants assert that for example, determining and displaying a probe similarity score and as another example, determining if unintended hybridization occurs. Applicant states that the presence of the unexpected properties is evidence of nonobviousness. Applicant contends that although the unexpected properties were unknown and non-inherent functions in view of Brown or Lockhart, since they do not inherently achieve the same results. Applicant states that in other words, theses advantages would not flow naturally from following their teachings, since Brown and Lockhart fail to suggest applying homology analysis among probes thereby determining and displaying probe similarity scores. Applicant further contends that the mere fact that one of skill in the art could apply homology analysis from "between a sample and a probe " to "between two probes" to meet the terms of the claims is not by instead sufficient to support a finding of obviousness. Applicant states that prior art must provide motivation or reason for one skilled in the art to provide the unexpected properties, such as determining a probe similarity score or

determining if unintended hybridization occurs, without the benefit of appellant's specification, to make the necessary changes in the reference device (*Ex parte Chicago Rawhide Mfg.* Co., 223 USPQ 351, 535 (Bd. Pat, App. & Inter. 1984). Finally, Applicants contend that neither Brown, Lockhart or Pal nor their combination teaches or discloses each and every feature of the presence invention as disclosed in independent claim 1. As such, the present invention as now claimed is distinguished and thereby allowable over the rejections raised in the Office Action. Applicants respectfully request withdrawal of all rejections.

Examiner's Response

10. All of the amendment and arguments filed on June 2, 2004 have been thoroughly reviewed and considered but are not found persuasive for the reasons that follow: In regards to Applicant arguments concerning the yeast expression analysis conducted by P. Browns groups, it is not clear the relevance of the arguments made by Applicant, since a prior art by P. Brown et al was not cited in the previous Office Action. Thus, the arguments against a prior art by P. Brown et al are deemed moot and will not be addressed by the Examiner. It is also noted that an attached explanatory drawing as indicated by Applicant was not found with Applicant's amendment and remarks. Accordingly, the Examiner did not consider the explanatory drawing and a response to the arguments therewith is not addressed by the Examiner.

In regards to Applicant's arguments that Lockhart et al does not teach or suggest "determining a probe similarity score" representing a similarity between first probe data on a base sequence of a least one of the probe biopolymer and a second probe data on a base sequence of at least one other of the probe biopolymer, so as to provide a visual indication of unexpected

or improper hybridization according to the invention, the Examiner respectfully disagree. Firstly, it noted that the Courts have established that during patent examination, the claims must be interpreted broadly as reasonably allow (*In re Zletz*, 893, F.2d 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989). In this case, Applicant has relied heavily on limitations wherein a "probe similarity score has been determined". However, neither the specification nor the claims provide a limiting definition of what constitutes "determining probes similarity score". The limitation in the claims does not necessarily include any type of algorithmic scoring programs. Therefore, "determining probes similarity score" can broadly be interpreted as "comparing hybridization or binding of multiple, different, unique probes on an array having some similarities or no similarities. Contrary to Applicant arguments, Lockhart et al meets this limitation. Lockhart teaches wherein the hybridization efficiency is compared between multiple, unique and different pairs of probes immobilized on a microarray, said probes having some similarities in base sequences[2] or possibly no similarities. Visual comparisons are made between the different probe pairs on the array (similarity score) and between the different pairs of probes and their target sample (hybridization intensities) (see figures). Thus Lockhart meets this limitation. Secondly, in regards to Applicant's arguments that Lockhart et al does not teach generating a visually intuitive graphical representation of the results, it is noted that Applicant has not provided a limiting definition in the claims or specification as to what encompasses a "visually-intuitive graphical representation" of results. While the specification at page 5, lines 20-23 discloses that "similarity patterns can be presented in a matrix-like form by arranging the subject probe biopolymers vertically and horizontally, which makes the displayed image more intuitive", it is not clear what

[2] Lockhart teaches on page 1676, wherein the array contained more than 16,000 different oligonucleotide probes (figure 2). Lockhart teaches wherein the oligonucleotide arrays contain collections of pairs of probes; each pair of probes having essentially the same base sequence, except

constitutes something becoming "visually-intuitive". In other words, it is unclear in the context of the claims how "visual" modifies "intuitive" or visa versa. Therefore, given the broadest, reasonable interpretation of the claim limitation, "a visually-intuitive graphical representation" of results can simply be interpreted as "a graphical display" as shown in the figures 2-5 of Lockhart et al at pages, 1676-1678, which is also visual. Thus, Lockhart meets this limitation. Thirdly, in regards to Applicant's arguments that the reference does not provide a visual indication of unexpected or improper hybridization, it is noted Lockhart does not exclude detecting unexpected or unknown hybridization in a sample. Specifically, Lockhart et al teaches blind spiking experiments (see page 1677, beginning at last paragraph of col. 1 to first six lines of col. 1 page 1678), wherein the hybridization intensities of unknown target in a complex RNA population are determined. Hence, the reference provides determination of "unexpected or unknown" hybridization intensities. Thus Lockhart et al meets the limitations of the instant invention.

In regards to Applicant's arguments that the reference of Pal et al fails to compensate for Lockhart's deficiencies since Pal does not disclose, teach or suggest at least displaying the "probe similarity score" along with the hybridization levels or intensities as disclosed or claimed for the present invention, it is noted that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, the secondary reference of Pal et al was not cited for its teaching of "a probe similarity score along with hybridization levels or intensities" for these teachings are

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for a single base difference.

found in the primary reference of Lockhart et al as previously discussed above. Rather, Pal et al was cited for its teaching of displaying hybridization intensities of signals with color differentiation and comparing different biochips (see Figures 3A-D; Figure 6A-D and col. 6, lines 24-36). As indicated in the prior Office Action of March 2, 2004, one of ordinary skill in the art would have been motivated to have applied Pal et al's multiple chips and color display techniques to the microarray of Lockhart et al for the benefits of visualizing differences in hybridization against a plurality of different samples. Likewise, it would have been *prima facie* obvious to one of ordinary skill in the art to have applied Pal et al's multiple chips and color displays to the method of detecting gene expression as taught by Lockhart et al for the advantages of analyzing many different samples simultaneously with the facility of visually distinguishing the sequence similarities. In regards to Applicant's arguments that the reference of Pal et al does not suggest generating a visually-intuitive graphical representation of the hybridization results, it is noted that neither the specification nor claims provide a limiting definition as to what constitutes a "visually-intuitive graphical representation" of hybridization results. Therefore as discussed earlier, the term "visually-intuitive graphical representation" is broadly being interpreted by the Examiner as a "visual graphical display", which is support by the teachings of both Lockhart et al and Pal et al. As shown in the teachings of Lockhart et al, Pal et al also depicts a visual graphical display of hybridization results in the teachings of Figures 3, 6, 7 and 8. Thus Pal et al meet this limitation. Applicant's arguments are not sufficient to overcome the rejections noted above. Accordingly, the rejections are maintained.

New Ground(s) of Rejections

THE NEW GROUND(S) OF REJECTIONS WERE NECESSITATED BY APPLICANT'S AMENDMENT AND BY APPLICANT'S SUBMISSION OF AN IDS UNDER 37 CFR 1.97(c):

Claim Rejections - 35 USC § 112

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 1-8 are indefinite at the recitation of "visually-intuitive graphical representation" because the specification or claims do not provide a limiting definition of the term and it cannot be determined what constitutes or encompasses a "visually-intuitive graphical representation". Likewise it is unclear within the context of the claims how "visual" modifies "intuitive" or visa versa. Clarification is required.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. *It is noted that Applicant has not provide a limiting definition for the term "visually-intuitive graphical representation". Accordingly the term is being interpreted by the Examiner as a "graphical display" that is visual.*

Claims 1-6 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Eisen et al (PNAS, Vol. 95, pages 14863-14868, December 1998). Regarding claim 1, Eisen et al teach a method of displaying results which a plurality of probe biopolymers are immobilized on a microarray are hybridized to a sample biopolymer, the method comprising determining information obtained in the hybridization experiment about a hybridization level for each of the probe biopolymers; determining probe similarity score representing a similarity between first probe data on a base sequence of at least one of the probe biopolymers and a second probe data on a base sequence of at least one other probe biopolymer; and displaying said information about the hybridization level for each of the probe biopolymers together with said probe similarity score, including generating a visual graphical representation of the determined hybridization level and correspondingly determined probe similarity score that may be intuitive to the biologist so as to provide at least one confirmation of similarities between the base sequences of corresponding biopolymers used in the hybridization experiments and a visual indication of any unexpected hybridization or any other functional information not currently available (see abstract and page 14863 last paragraph of col. 1 to col. 2, lines 1-8, 28-43 and page 14864, entire section entitled "Materials and Methods".

Regarding claim 2, Eisen et al teach the method of claim 1 for display results of a hybridization experiment, wherein said step of generating the visually-intuitive graphical representation include assigning different depths in a color to different values of the probe similarity (page 14864, sections entitled "Metrics", "Hierarchical Clustering" and "Display").

Regarding claim 3, Eisen et al teach the method of claim 1 for displaying results of a hybridization experiment, wherein said step of generating the visually-intuitive graphical representation include assigning different depths in a color to different values of the probe similarity score, and arranging subject probe biopolymer horizontally and vertically to form a matrix (page 14864, sections entitled "Metrics", "Hierarchical Clustering" and "Display").

Regarding claim 4, Eisen et al teach the method according to any one of claims 1-3 for displaying hybridization results, wherein said step of generating the visually-intuitive graphical representation includes displaying the information about the hybridization level by assigning different depths in color to different values of the hybridization level (page 14864, sections entitled "Metrics", "Hierarchical Clustering" and "Display").

Regarding claims 5, Eisen et al teach the method according to any one of claims 1-3 for displaying hybridization results, wherein probe biopolymer data, hybridization levels and probe similarity scores are displayed sided by side by sorting then by values of the probe similarity score between specific one of the probe biopolymers and each of the probe biopolymers. Likewise, Eisen et al teach wherein a profile of changes in the hybridization level of the subject biopolymers on the (page 14864, sections entitled "Metrics", "Hierarchical Clustering" and "Display"; section entitled "Redundant Representations of Gene Cluster Together" and Figures 1 and 2).

Regarding claims 6, Eisen et al teach the method according to claims 5 for displaying results of hybridization experiments, wherein the hybridization levels or hybridization profiles are analyzed on a plurality of different microarrays (biochips) and wherein the hybridization profiles are displayed side by side (page 14867, Figure 3).

Regarding claim 8, Eisen et al teach the method according to claim 1 for displaying results of a hybridization experiment according to claim 1, wherein the probe data on the base sequence of the probe biopolymers for determining the probe similarity score includes at least one of DNA probes names and DNA probe definition information (see Figure 2). Therefore, Eisen et al teach the limitations of claims 1-6 and 8 of the instant invention.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Eisen et al as applied to claims 1-6 and 8 above, and further in view of Lockhart et al (Nature Biotechnology, vol. 14, pages 1675-1680, December 1996). Regarding claim 7, Eisen et al teach a method according claim 6 for displaying results of a hybridization experiment, wherein the hybridization

levels obtained from a plurality of microarray are displayed side by side (see figure 3). Eisen et al differs from the instant invention in that the reference does not teach wherein a profile of changes in the hybridization level of the subject biopolymer on the plurality of biochips is statistically analyzed and the results of the analysis are displayed together with the results of clustering the probe biopolymer.

Lockhart teach a method similar to that of Lockhart for displaying the results of a hybridization experiment, the method comprising the step of displaying information obtained in hybridization experiments about a hybridization level for each probe (see whole document teaching arrays with measuring level of hybridization signal (see figure 3 and 5 and their teaching of phycoerythrin and fluorescein emission in experimental protocol). Lockhart et al teach that the array contains over 65,000 different oligonucleotide probes (see page 1678). Lockhart et al teach wherein a profile of changes in a hybridization level of a subject biopolymer(s) is statistically analyzed (quantitated) and the results of the analysis displayed along with clustering information of the probe biopolymers (see Figures 3-4 for statistical analysis and Figures 2 and 5 for clustering data). Lockhart et al teach that statistical analysis of expression level along with clustering information (quantitative monitoring) proves valuable in elucidating gene function, exploring the causes and mechanisms of diseases and for the discovery of potential therapeutics and diagnostic targets (page 1679, col. 1, second full paragraph). Therefore, one of ordinary skill in the art at the time of the claimed invention would have been motivated to have modified the display method of Eisen et al to further encompass results from a statistical analysis as taught by Lockhart et al for the benefits of providing additionally information which may be valuable in elucidating gene function, exploring the

causes and mechanisms of diseases and for the discovery of potential therapeutics and diagnostic targets as suggested by Lockhart et al. Likewise, it would have been *prima facie* obvious to apply Lockhart's method of statistical analysis with Eisen's method of displaying clustering of probe biopolymers in order to further enhance visually distinguishing sequence similarities and hybridization intensities.

Conclusion

17. No claims are allowed. Applicant's amendment and submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on June 2, 2004 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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